

## PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number

Q96974

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on \_\_\_\_\_

Signature

Typed or printed name

Application Number  
10/599,203

Filed  
September 22, 2006

Confirmation Number: 5777

First Named Inventor  
Yoshinobu YAMAZAKI

Art Unit  
1628

Examiner  
PAGONAKIS, ANNA

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a Notice of Appeal.

The review is requested for the reason(s) stated on the attached sheet(s).

Note: No more than five (5) pages may be provided.

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### CORRESPONDENCE ADDRESS

Direct all correspondence to the address for SUGHRUE MION, PLLC filed under the Customer Number listed below:

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I am the

applicant/inventor.

assignee of record of the entire interest. See 37 CFR 3.71.

Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)

attorney or agent of record.  
Registration number 40,641

attorney or agent acting under 37 CFR 1.34.  
Registration number if acting under 37 CFR 1.34 \_\_\_\_\_

  
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April 8, 2011

Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below\*.

\*Total of 1 form is submitted.

**PATENT APPLICATION**

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of

Docket No: Q96974

Yoshinobu YAMAZAKI, et al.

Appln. No.: 10/599,203

Group Art Unit: 1628

Confirmation No.: 5777

Examiner: PAGONAKIS, ANNA

Filed: September 22, 2006

For: MEDICINE FOR PREVENTION OR TREATMENT OF FREQUENT URINATION OR  
URINARY INCONTINENCE

**PRE-APPEAL BRIEF REQUEST FOR REVIEW**

**MAIL STOP AF - PATENTS**

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Sir:

Pursuant to the Pre-Appeal Brief Conference Pilot Program, and further to the Examiner's Final Office Action dated December 9, 2010, Applicant files this Pre-Appeal Brief Request for Review. This Request is also accompanied by the filing of a Notice of Appeal.

Applicant turns now to the rejections at issue:

Claims 11-12 and 17 are the only claims pending in the application and are rejected under 35 U.S.C. § 103(a) as being allegedly unpatentable over Tanaka et al. in view of Garvey et al. as evidenced by Mesh Supplementary Data and further in view of Guittard et al. and Sigurdsson (US 6,132,365).

Applicants respectfully traverse the rejections for the reasons of record, which are incorporated herein by reference, and submit that (1) the Examiner has not made a *prima facie* showing of obviousness as there is no apparent reason to combine the references as suggested by the Examiner with a reasonable expectation of success in achieving the claimed invention; and (2) the Examiner has failed to give proper consideration to the arguments presented in the Response filed February 9, 2011 in conjunction with claim language, the previous arguments of record and the data provided in the specification as errors to be reviewed.

The present claims recite a method for the treatment of urinary frequency or incontinence, comprising administering to a subject having urinary frequency or incontinence accompanied with neurogenic bladder dysfunction, unstable bladder, bladder spasm, chronic or acute prostatitis, a combination consisting essentially of a (1) phenoxyacetic acid derivative represented by formula (I), or a pharmaceutically acceptable salt thereof and (2) silodosin or a pharmaceutically acceptable salt thereof.

As pointed out in the Remarks of the Amendment filed November 24, 2010, the teachings of Tanaka and Garvey et al. do not provide a reason to a person having ordinary skill in the art to use silodosin in combination with a phenoxyacetic acid derivative (I) of the presently claimed invention for treating urinary frequency or incontinence accompanied with neurogenic bladder dysfunction, unstable bladder, bladder spasm, chronic or acute cystitis or chronic or acute prostatitis.

Garvey et al. relates to a composition and method for treating overactive bladder comprising administering a compound of claim 1, at least one compound that donates nitric oxide or the like (claim 17) and further at least one vasoactive agent (at least three compounds). Thus, the composition and method of Garvey are different from the claimed invention and one of ordinary skill in the art would not have been motivated to modify or combine the teachings of Garvey et al and Tanaka to arrive at the claimed invention. Sigurdsson does not remedy this deficiency or teach anything that would motivate one of ordinary skill in the art to modify the combination or method of Tanaka and Garvey et al., even if combined, to arrive at the claimed invention.

Garvey et al. mentions urge incontinence and overactive bladder as conditions that may be treated, however, there is no example of such treatment and no guidance or suggestion as to which of the many potential combinations of agents suggested might have been considered for the treatment of these particular conditions amongst all of the conditions listed. There is no data supporting the effect of such a combination with respect to overactive bladder. Thus, one of ordinary skill in the art would not have been motivated to use silodosin for the treatment of urinary frequency or incontinence with a reasonable expectation of success based on the teachings of Tanaka and Garvey et al. Sigurdsson does not remedy this deficiency or teach

anything that would motivate one of ordinary skill in the art to modify the combination or method of Tanaka and Garvey et al., even if combined.

Mesh Supplementary Data is relied on as teaching that KMD-3213 is an alternative name for silodosin, which is not disputed.

The Examiner relies on Guittard et al primarily for the teaching of a relationship between urge incontinence and overactive bladder. However, Applicants submit that the teaching by Guittard et al that "involuntary urinary incontinence is also known as urge incontinence and overactive bladder" is incorrect. Urinary incontinence and overactive bladder are not the same.

Sigurdsson merely states that urinary incontinence is caused either by involuntary muscle contractions of the bladder muscle (so called unstable bladder) or by insufficient contraction of the urethral sphincter muscle. Sigurdsson also teaches that unstable bladder can be treated with medication or bladder training. Column 1, lines 38-39. However, that fact that urinary incontinence may be caused by unstable bladder or may be treated with medication is not in dispute. Moreover, the teachings of Sigurdsson do not add anything to the other cited references which might motivate one of ordinary skill in the art to modify or combine the references and employ the specifically claimed combination *consisting essentially of* (1) a phenoxyacetic acid derivative of formula (I) and silodosin of the presently claimed invention for treating urinary frequency or incontinence accompanied with neurogenic bladder dysfunction, unstable bladder, bladder spasm, chronic or acute cystitis or chronic or acute prostatitis.

Even further, Sigurdsson is related to a non-pharmacological approach to urinary incontinence caused by a weak or damaged sphincter muscle, which is not related to the present invention or any other pharmacological treatment methods at all. Moreover, Sigurdsson does not provide any teachings or disclosure to refute Applicants' evidence of unexpected results regarding the present invention. As previously pointed out, the results in the specification show the direct effect of improvement of urinary frequency of silodosin, not a secondary effect by inhibiting contraction of urethra. Sigurdsson is not at all related to a pharmacological method of treatment and does not refute Applicants' evidence of unexpectedly superior results.

Thus, Applicants have shown that (1) the teachings of Tanaka and Garvey et al do not provide a reason to a person having ordinary skill in the art to use silodosin alone or in combination with a phenoxyacetic acid derivative (I) of the presently claimed invention for

treating urinary frequency or incontinence accompanied with neurogenic bladder dysfunction, unstable bladder, bladder spasm, chronic or acute cystitis or chronic or acute prostatitis as recited in the present claims; and (2) the unexpected results obtained by the presently claimed invention rebut any *prima facie* case of obviousness that may have been set forth.

In the Advisory Action mailed February 25, 2011, the Examiner appears to indicate that since Applicants did not discuss evidence of unexpected results in detail in the Response filed February 9, 2011, that such evidence is not considered persuasive. This is in error since Applicants refer to the data in the specification as showing the direct effect of improvement of urinary frequency of silodosin, not a secondary effect by inhibiting contraction of urethra, which is discussed in detail in the previous Responses filed. Thus, the Examiner should consider the entire record including the data provided in the specification and previous Responses filed.

Further the Examiner indicates that the rejection made under 35 U.S.C. §103(a) is based upon the combination of references and not an individual reference alone. In this regard, the Examiner characterizes Applicants' argument as taking the position that, because Garvey et al. discloses compounds in addition to the one instantly claimed, this somehow constitutes a complete lack of teaching of the claimed compound and/or constitutes a teaching away from the instantly claimed compound. In response, the Examiner states that the disclosure of a reference is not limited to that which is preferred or exemplified. Thus, the Examiner states that the fact that other compounds may be exemplified, claimed and/or preferred does not negate or direct the artisan away from the broader teaching of the reference, which expressly provides for, and thus, clearly contemplates the use of instantly claimed compound.

This also in error because the composition of Garvey requires three elements and it is improper for the Examiner to pick some of the elements of the composition to combine with teachings of another reference, particularly in view of the claim language which recites that the present invention involves a combination of agents consisting essentially of (1) a phenoxyacetic acid derivative represented by a general formula (I) and (2) silodosin. The language "consisting essentially of" excludes additional ingredients not claimed which adversely affect the basic and novel characteristics of the claimed invention. This point was addressed in detail in the Response filed November 24, 2010 and the data provided in the specification indicates that the

claimed composition provides unexpectedly superior results as discussed above. Thus, the present claims exclude additional ingredients such as those taught in the composition of Garvey et al, which adversely affect the basic and novel characteristics of the claimed invention.

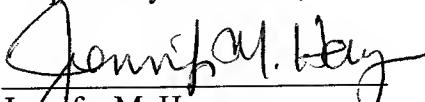
Namely, in the micturition interval measurement as shown in Example 2 of the present specification, the inventors used the acetic acid-stimulated frequency model, which is a frequency model independent of the presence or absence of urinary obstruction. Therefore, the results on silodosin show the direct effect improving urinary frequency of silodosin, not a secondary effect by inhibiting contraction of urethra.

Thus, the teachings of the cited references, whether taken alone or in combination, do not provide a reason to a person having ordinary skill in the art to use a combination *consisting essentially of* (1) a phenoxyacetic acid derivative (I) and (2) silodosin as in the presently claimed invention for treating urinary frequency or incontinence in a subject having urinary frequency or incontinence accompanied with neurogenic bladder dysfunction, unstable bladder, bladder spasm, chronic or acute cystitis or chronic or acute prostatitis. For at least this reason, the present invention is not rendered obvious by the cited references.

In addition, the specific combination of silodosin and the phenoxyacetic acid derivative of the formula (I) of the present invention exerts the unexpectedly synergic effect as shown based on the experimental data provided in the specification as discussed in detail in the Response of record. For this additional reason, the present invention is patentable over the cited references.

Accordingly, Appellants respectfully request the Pre-Appeal Brief Conference Panel to withdraw the foregoing rejections in view of clear error.

Respectfully submitted,



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